

### **REMARKS**

Claims 50, 52, 55-63, 65-68, 70 and 72-79 are pending. Claims 80 and 81 are presently canceled herewith without disclaimer of any subject matter. The right to file subsequent applications to such subject matter is reserved. Claims 50, 60, 63, 65-68, 70, 73-79 are presently amended.

Support for the claim amendment can be found throughout the specification including the Drawings and Claims as filed originally.

In particular, claim 50 has been amended to more particularly point out the featured mammal. Specific support for the amendment can be found at pgs. 7-8, bridging paragraph for instance.

Claims 60, 63, 65-68, 70, and 73-79 have been amended to improve claim clarity and/or dependency.

No new matter has been added by virtue of the present amendment.

Claim 81 stands rejected as being anticipated over various references under 35 USC §102 at pg. 2 of the Action. While Applicants respectfully disagree with the position taken, basis for it has been addressed by this amendment. Reconsideration and withdrawal are requested.

Claims 50-52, 55-63, 65-68, 70, 72-79, and 81 stand rejected as obvious over Hammond et al. (US Pat. No. 5,880,090) in view of Asahara et al. (*Science* 275: 964 (1997)) or Isner (U.S. Pat. No. 5,980,887. Applicants traverse for reasons already of record and further in view of the

presently submitted Declaration of Takayuki Asahara under 37 CFR 1.131 ("Declaration"). Takayuki Asahara (Dr. Asahara) and Dr. Jeffery Isner (Dr. Isner) are the co-inventors of the instant application.

Consideration of the Declaration at the present time is respectfully requested.

The Declaration establishes, among other things, that the present inventors conceived and reduced the claimed invention to practice in the United States well in advance of September 19, 1997. That date is the 102(e) date shown on the face of the Hammond patent. Accordingly, Applicants have antedated Hammond and request withdrawal of the patent as a reference.

In particular, the Declaration establishes that well before September 19, 1997 the inventors of the present application prepared a draft manuscript entitled *Regulation of Neovascularization with Ischemia- or Cytokine-induced Mobilization of Bone Marrow-derived Endothelial Progenitor Cells* ("Manuscript") Decl. at ¶ 6. According to Dr. Asahara, the Manuscript reports results of experiments in which the inventors induced formation of new blood vessels in subject mammals by administering granulocyte-macrophage colony stimulating factor (GM-CSF). Decl. at ¶ 6.

More specifically, Dr. Asahara states that well before September 19, 1997, he and Dr. Isner administered GM-CSF to rabbits before ischemic surgery. Decl. at ¶ 7. Extensive induction of new blood vessel growth and better ischemic limb blood pressure was observed in ischemic rabbits following this treatment. Decl. at ¶ 7-8. Both inventors understood that GM-CSF administration could be used to induce new blood vessel growth in mammals to treat ischemic vascular disease. Decl. at ¶ 9.

Dr. Asahara also states that well before September 19, 1997, he and Dr. Isner induced

formation of new blood vessels in mice cornea by administering GM-CSF. Decl. at ¶ 8.

Well before September 19, 1997, Dr. Asahara states that he and Dr. Isner developed assays to monitor induction of new blood vessel growth that followed administration of GM-CSF to subjects. These assays included a rabbit ischemic hindlimb model, mouse corneal neovascular assay model, and methods for assessing vessel density and capillary/muscle fiber ratios. Decl. at ¶ 10-12.

In particular, Dr. Ashara states that well before September 19, 1997, he and Dr. Isner administered recombinant human GM-CSF before and after induction of ischemia in rabbits. Decl. at ¶ 13-15.

Well before September 19, 1997, Dr. Ashara states that he and Dr. Isner analyzed results obtained from administering GM-CSF to ischemic mammals to induce new blood vessel growth. Formation of such new blood vessels by the method was observed. Decl. at ¶ 16-17.

Dr. Asahara further states that before September 19, 1997 he and his co-inventor Dr. Isner conceived of and practiced the claimed method of inducing formation of new blood vessels in subject mammals by administering GM-CSF. Decl. ¶ 18.

Dr. Isner is deceased as evidenced by the attached obituary notice from *The Boston Globe* newspaper dated November 1, 2001. Accordingly, Dr. Ashara as the surviving inventor is entitled to execute the Declaration and have that document fully considered by the USPTO without Dr. Isner's signature. See MPEP 715.05.

In view of the foregoing, it is clear that the present inventors conceived of and practice the claimed invention before Hammond's 102(e) date. Withdrawal of the Hammond patent as a

reference is requested at this time.

None of the other cited references, remedies the deficiencies in the rejection particularly those apparent after withdrawal of Hammond. In view thereof, reconsideration and withdrawal of the rejection are respectfully requested.

The Declaration is unsigned. Applicants will send the Office a signed Declaration under separate cover.

Claims 50 and 81 stand rejected as being anticipated under 35 USC 102(b) by Takeshita et al. (*J. Clin. Invest.* 93: 662 (1994)). While Applicants respectfully disagree with the stated reasons for the rejection, basis for it has been addressed by this submission.

In particular, claim 50 has been amended so that the featured mammal is a **rodent or primate**. As cited, Takeshita et al. reports use of a **rabbit** to practice a therapeutic method. Action at pg. 8. Since a rabbit is not a rodent or a primate, there is no basis for an anticipation rejection in view of Takeshita et al. as relied on.

Claim 81 has been canceled.

In view thereof, reconsideration and withdrawal of the instant 102(b) rejection are requested.

### **CONCLUSION**

Applicants submit that all claims are allowable as written and respectfully request early favorable action by the Examiner. If the Examiner believes that a telephone conversation with Applicants' attorney would expedite prosecution of this application, the Examiner is cordially

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invited to call the undersigned attorney of record.

Although it is not believed that any fee is needed to consider this submission, the Examiner is authorized to charge our Deposit Account No. 04-1105 should such fee be deemed necessary.

Date: 17 OCT 2003

Respectfully submitted,



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